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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,360	09/04/2001	Teruaki Sekine	2001_1248A	1329

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,360	SEKINE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 24-35 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

Claims 30-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing recurrence of liver cancer for five years, does not reasonably provide enablement for a method for preventing recurrence of "cancer" for five years. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 30-35 are drawn to a method for preventing recurrence of cancer for five years, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

Claims 30-35 encompass a method for preventing recurrence of "any cancer" for five years, comprising administering activated lymphocytes while performing treatment of cancer, which is surgical operation.

The specification discloses that the rate of recurrence of liver cancer when checked in 5 years after administering activated lymphocytes within three weeks and

after three and six months after performing operation of the liver cancer, is significantly lower than the control (p.12-13).

In the instant response, Applicant argues that claimed method is also effective in preventing recurrence of glioblastoma up to 132 months.

One cannot extrapolate the teaching of the specification to the scope of the claims because different cancers have different etiology and characteristics, and one cannot predict whether different cancers would have the same response to the same drugs. For example, Montesano, R et al,1996, Intl J Cancer, 69(3): 225-235, teach that two different forms of esophagus cancer, squamous cell carcinoma (SCC) and adenocarcinoma (ADC) have different etiological and pathological characteristics, and that a comparison of p53 mutations in these two cancers shows that said mutations differ by their types, frequencies, distribution along the gene and impact on p53 protein structure (p.231, second column, first paragraph). Similarly, Burmer, GC et al, 1991, Environmental Health perspectives, 93: 27-31, teach that in contrast to sporadic colon carcinomas, mutations in c-Ki-ras are infrequently observed in carcinomas or areas of high-grade dysplasia in patients with chronic ulcerative colitis, and that differences in the frequency, and spectrum of mutations observed in sporadic colon carcinoma and pancreatic carcinoma suggest that a different class of carcinogens may be involved in the initiation of these two tumors (p.27, second column, last paragraph, bridging p.28). Busken, C et al, Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No:850, teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between

adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract).

Thus based on the teaching in the art and in the specification, one cannot predict that recurrence of any cancer could be prevented by the claimed method.

The specification lacks guidance on the dosage, frequency of treatment and assessment of any cancer.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

REJECTION UNDER 35 USC 103

Claims 24-35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sekine T, 1994, Human cell: Official J human cell res society (Japan): 7(3): 121-4, of record, in view of Sasaki Y et al, J Hepato-biliary-pancreatic surgery, 1998, 5(1): 14-17, for reasons already of record in paper of 03/03/05.

Applicant argues that the claimed prevention of recurrence of liver cancer for at least five years could not have been suggested by Sekine reference, which only teaches prevention of recurrence of liver cancer for two years.

Applicant argues that the expected 5-year survival taught by Sasaki et al is the over-all survival, which is different from the recurrent-free survival, in that the survival curve in recurrent –free survival drops with recurrence during the period of observation, whereas the survival curve in overall survival is invariable, but drops with fatal cases.

Applicant argues that the expected 5-year survival is inconsistent with the high recurrence rates disclosed in Sekine, which is 33% for recurrence of liver in the first year, 57% in the second year, and 70% in the third year, and that no effective preventative method is known. Applicant argues that in this sense, Sekine teaches away from the claimed method for prevention for 5 years, and that no reasonable expectation of success existed at the time of the publication of Sekine for the prevention of recurrence of liver cancer or cancer in general for five years.

Applicant argues that on the contrary, the claimed invention is surprising and unexpected results.

Applicant argues that antitumor activity of administered activated LAK cells, as taught by Osband et al, 1990, lasted only for a short period of about two years.

Applicant's arguments in paper of 07/05/05 have been considered but are found not to be persuasive for the following reasons:

Although Sekine only teaches prevention of recurrence of liver cancer for two years, one would have expected that the method of Sekine et al, using activated lymphocytes would prevent recurrence of liver cancer for five years, in view of the teaching of Sekine et al that from previous experimental administration, they knew that higher preventive effect could be obtained if the infusion were carried out more frequently and continuously after an operation, and that the currently used dosage is a minimum dosage (p.7, first paragraph under conclusion). It is noted that to determine optimum concentration of reactants is within the level of ordinary skill in the art. See In re Kronig, 190 USPQ 425.

Further some recurrent liver cancer is not fatal, and would not be counted in over-all survival rate, and thus not all patients in over-all survival group are expected to have recurrent liver cancer, in view of the teaching of Sekine et al that out of 52 cases, there are 22 recurrence cases and 6 deaths in the second year (abstract). Thus in view that liver cancer patients with hepatectomy alone could survive not only 5 years at a rate of 32% , but even 10 years at a rate of 23% for patient having bad liver function at the time of surgery, as taught by Sasaki et al, one would have expected that some patients having hepatectomy and treated with activated lymphocytes, as taught by Sekine et al, would not have recurrent liver cancer for at least 5 years.

Moreover, contrary to Applicant's argument, Sekine does not teach away from the claimed method for prevention for 5 years. The expected 5-year survival of 32 % is not inconsistent with the high recurrence rates disclosed in Sekine, which is 33% for recurrence of liver cancer in the first year, 57% in the second year, and 70% in the third year, because they are data at from different year, and because for the third year, 70% with recurrent liver cancer means 30% would not have recurrent liver cancer, and thus at least 30% or more are survival, when considering not all recurrent liver cancers are fatal.

Concerning the antitumor activity of administered activated LAK cells, one cannot extrapolate the effects of LAK cells against lung carcinoma to the effect of the activated lymphocytes on liver cancer, because they are different diseases, with unpredictable responses to the same drug.

Applicant further argues that claimed method is also effective in preventing recurrence of glioblastoma up to 132 months.

Applicant's arguments in paper of 07/05/05 have been considered but are found not to be persuasive for the following reasons:

The claims are not limited to glioblastoma, and thus they are still obvious in view of the combined teaching in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

August 09, 2005